Ted,

Based on biomarker selection criteria recommended by National Research Council and Dr. Neil Benowitz, we selected nicotine and 5 metabolites (i.e., nicotine-*N*-glucuronide, cotinine, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine, and *trans*-3'-hydroxycotinine-*O*-glucuronide) as biomarkers of exposure to cigarette smoke. Studies indicated that the measurement of 24-hour urinary nicotine and 5 metabolites reflects about 80% of ingested nicotine. (I verified this information with Shxia.)

With regard to the topography device, the sensitivity of the device is such that human smoking is typically well characterized. However, this assumes crossing a certain threshold (i.e., approximately 17 – 20 mL/second). Formulating a puff smaller than that (especially if the puff is taken at a very slow rate) will either be truncated or not detected at all. As I recall, engineers at Ashland found that about 5% of puffs that were taken were not detected using the topography device. However, their smokers typically mimicked FTC methods when smoking (i.e., 35 mL volume; 2 second duration). We already know that FTC does not nor was it intended to reflect how humans smoke. Nevertheless, if we are missing 5% of puffs taken yet we average puff volume, duration, etc., we will overestimate our parameters.

Hope this helps.

Candace